Pediatric Environmental Health

Bailus Walker Jr, PhD, MPH, FACE
Washington, DC

The links between environmental agents, environmental conditions, and disease and disability among children are receiving increasing attention. Evidence abounds that children are more susceptible than adults to the damaging effects of environmental agents and conditions. This evidence is illuminated by the much-publicized and expanding research agenda on the prevention, recognition, diagnosis and treatment of environmentally related disease in the pediatric population. Encouragingly, advances in molecular biology and other sciences are providing important tools to aid pediatricians and other healthcare professionals in meeting the environmental health needs of children.

Key words: pediatric ■ environmental health

 From the Environmental and Occupational Medicine program, Department of Community Health and Family Practice, Howard University Medical Center, Washington, DC. Send correspondence and reprint requests for *J Natl Med Assoc.* 2005;97:262–269 to: Bailus Walker, PhD, Department of Community Health and Family Practice, Howard University Medical Center, Mudd Building, Suite 2400, 520 W St. NW, Washington, DC 20059.

The links between environmental contaminants, environmental conditions and childhood disease and disability are attracting far more attention than in the past. First, biomedical science is advancing on multiple fronts—and public awareness of the issue has grown—not just in the U.S. medical community but all around the globe. Patients and parents are increasingly raising questions about environmental effects with their physicians. Similar concerns have been the focus of symposia and multiauthored publications. Of particular interest are environmental exposures experienced by children in urban centers because of the broad spectrum of environmental health risks (physical, chemical, biological, social), facing this group. This attention cannot be explained by one cataclysmic event.

Rather, a more complex convergence of multiple and intertwined influences has elevated into sharper focus the adverse health effects of environmental exposure on children. For instance, asthma, childhood cancer, neurodevelopmental disorders and endocrine dysfunctions are among the diseases of the pediatric population for which there are environmental components. Moreover, certain early stages of development or the "critical window" exposure to an environmental toxicant can have more severe consequences than would a similar exposure in adulthood.

Unfortunately, in the past, children have not been included in the environmental health risk assessment processes of regulatory agencies, and most environmental regulations were based on environmental exposure data from adult males. Also, in the past, the educational system paid scant attention to environmental factors that may have interfered with a student's ability to progress through the required coursework. But there is now increasing biomedical momentum to study the environmental determinants of children's health, with new academic centers and research organizations devoting more intellectual resources to the issue.

At the same time, there is concern that available scientific evidence of environmental influences on health and disease is not being translated and incorporated into standard pediatric practice. For

instance, researchers[1] at the Children's Hospital Oakland (CA) Research Institute report that if one reviews the medical records in many large children's hospitals, the paucity of information on environmental agents rapidly becomes evident. The researchers report that when the medical records of children evaluated for respiratory illness were reviewed, fewer than 10% of the records indicated that questions were asked about exposure to passive cigarette smoke. Similarly, in patients presenting with behavioral problems and developmental irregularities, records seldom indicate test for blood lead levels or other environmental neurotoxins. Others have raised concerns about this lack of attention to environmental issues in health clinics. These discussions have been spurred in many instances by an array of public health, legal (including lawsuits) and social issues for which pediatric environmental health data from clinical experience would have been of value in addressing the problems at hand.

Evidence abounds that when healthcare providers fail to ask patients about environmental exposures and related risk factors, environmentally related disorders may be incorrectly attributed to nonenvironmental causes, unnecessary tests may be ordered, and patients may be referred to consultants equally unprepared to connect environmentally related exposure to disease. All of these add to stress on the child as a patient and on his/her family and may have broader societal ramifications. Part of the problem is described by the American Academy of Pediatrics' Committee on Environmental Health:[2] *"Until recently, however, most physicians and nurses received only limited training in evaluating possible environmental triggers of illness in their patients."*

This review highlights selected issues relevant to the prevention, treatment and eradication of pediatric environmental health problems in the 21st century. The objective is basically to take stock of the known and unknown and, at the same time, increase awareness of environmental issues to be addressed within clinical pediatrics.

Environment

Before considering specific environmental risk factors, it is necessary to consider definitions and concepts of the environment, an elastic term. A number of definitions and methods of measuring "the environment" have been developed. There are also different disciplinary perspectives on the term. The environment for most epidemiologists comprises everything that is not genetic. Although no single definition of the environment is without its deficiencies, each offers benefits in terms of perspectives and understanding.

The human system has two environments, separated by three principal protective barriers: skin, gastrointestinal tract and the membranes within the lungs. Although they may provide protection, each of these barriers is vulnerable under certain conditions. Childs,[3] in writing on gene-environment interaction, describes the inner environment as consisting of the organized structure of cells, including the apparatus of physiological homeostasis. The engines of these qualities, the proteins, originate in the genes, which themselves are subject to organizing principles. Then, there is the personal (use of tobacco, drugs, diet) environment, which the individual can control, and the ambient environment, over which the individual has no control. The environment can also be considered as existing in three forms—gaseous, liquid and solid. Each is subject to pollution, and children interact with all of them. Another perspective considers the environment in terms of four avenues—chemical, biological, physical (noise, ionizing radiation, pressure) and socioeconomic factors—or mechanisms by which various factors affect people. Unfortunately, the socioeconomic factors have not been measured and evaluated as extensively as human-made physical and chemical factors. Yet, a better understanding of the pathways by which socioeconomic factors contribute to illness can enhance efforts to prevent disease and premature death among children.

Exposure

No matter how hazardous environmental agents or conditions are, without exposure, there is no risk, and environmental exposure data are critical to diagnostic inferences. Stages of development, patterns of time use and activity place children in diverse environments throughout the day, each setting possibly having its own unique spectrum of environmental toxicants. What follows is a description of sources and pathways of exposure with primary focus on environmental toxicants.

Children have disproportionately heavy exposure to environmental toxicants. Such exposure may occur through numerous routes, including food; air; soil; dust; and other nonfood items, such as consumer products. Children drink more water, eat more food and breathe more air pound-for-pound of body weight compared with adults. Some children work in crop production and in other labor services, for example, and may be exposed through the occupational route. Working parents may also expose children to contaminants (i.e., asbestos) through contaminated work clothes or contaminated automobiles driven to and from work. Then, there is exposure in the school environment, which is a different physical environment than the residential setting. Urban schools are frequently located near highways, where exposure to motor vehicle emissions can be significant.

Although environmental measurements in air, water, soil or food are often used as surrogates for exposure, they represent "potential" exposure rather than "actual" exposure. Even though the potential for exposure may be the same, not all potentially exposed children will experience the same actual exposure.

Clearly, children are exposed to mixtures, not single environmental toxicants. This raises concerns about the potential for synergistic, or more than additive, effects. In this case, the effects of two substances together are greater than the sum of either alone. This interaction may include medications, which are beneficial to human health but have the potential to act on other environmental substances. What is more, many medications used routinely to treat children have not been proven to be safe and effective for the pediatric population. Only a third of the medicines used to treat children have been studied adequately in the pediatric population.[4]

Fetal Exposure

Exposures may occur at stages of development not frequently considered in clinical assessments, such as before conception. For example, women inadequately treated for plumbism in childhood may give birth to infants with congenital lead poisoning. The toxicokinetic explanation for this type of exposure is that storage of lead in bone is mobilized during pregnancy. Lead accumulation in fetal tissue, including brain, is proportional to maternal blood lead levels. Another example of exposure prior to conception is women who conceived after eating cooking oil contaminated with polychlorinated biphenyls (PCB) gave birth to infants with "Yusho" (oil disease). Yusho was essentially chloracne, familiar to occupational medicine specialists as "cable handler's itch" from the linear puritic band it produced at points of contact with insulated or impregnated cable.[5,6]

Exposures of the fetus, which in most instances are dependent on the mother, can represent excessive conditions or a deficiency, such as low levels of folates that can increase the risk of serious birth defects of the spine and brain. Excessive ethanol in the fetal environment can interfere with delicate nervous system wiring, a process easily disrupted during rapid growth and development before and after birth.

Excessive exposure to pesticides may also increase the risk of adverse neurodevelopment sequelae in offspring. In fact, prenatal exposure to organophosphate pesticides may be more dangerous than previously thought, because acetyl cholinesterase may have a direct role in neuronal differentiation. In urban centers, widespread pesticide exposure is common. These pesticide uses are often necessary because the urban landscape, including poor housing maintenance, inadequate municipal services, such as waste collection and street cleaning, can be conducive for insect and animal (rats) pests. Whyatt's group[7] found widespread pesticide use and exposure during pregnancy among a cohort of African-American and Dominican women in New York City. Specifically, 85% of the women report that pest control measures were used in homes during pregnancy. Pesticides were detected in the biological samples of all women monitored during the third trimester. This study adds to the weight of evidence of widespread residential pesticide use nationwide. Such use is not limited to agricultural communities.

Aldridge's group[8] determined that fetal or neonatal exposure to an organophosphate pesticide alters the program for the development of serotonin synaptic function, thus, affecting the serotonin system in later stages of development and extending the effects of the pesticide beyond cholinergic neurotransmission. Serotonergic dysfunction is involved in appetitive and affective disorders. These disturbances apparently have contributions from environmental neurotoxin exposures.

It bears repeating that nervous system development is especially vulnerable to environmental interference, because the process involves the production of billions of nerve cells and trillion of glial cells, which must follow precise choreography: migration, synaptogenesis, selective cell loss and myelination.[9] Environmentally induced disruption of any one step in this process can have serious, long-term consequences. Equally important, environmental agents that target and injure blood and the hematopoietic system or liver, kidneys or lung may secondarily affect a child's neurological function. Parenthetically, a growing body of evidence indicates that the social and economic impact of neurological and developmental disorder (e.g., attention-deficit disorders and ADHD-like symptoms) is large and increasing.[10]

A relatively recent concern is developmental effects of in utero exposure to phthalates. Phthalates are a family of multifunctional chemicals, which are widely used in many diverse products, such as plasticizers for polyvinylchloride (PVC) formulations in several applications: medical devices, toys, food wraps and building products. Phthalates vary in their ability to induce the following effects: liver injury, liver cancer and antiandrogenic activity. Because phthalates do not bind with the plastic, they leach with time and use from vinyl products, thus, becoming a ubiquitous environmental contaminant. Phthalates are present in residential air, and exposure to phthalates can occur via inhalation, ingestion and dermal routes, as well as through medical devices containing phthalates. Also, medications, tablets, capsules and other preparations taken chronically can be a source of phthalate exposure. The proportional contribution of medications to a child's total

phthalate exposure is not known. Detectable levels of di (2-ethylhexyl) phthalate (DEHP) have been observed in a wide population of newborns. Phthalate exposure is both higher and more common than previously suspected. Pregnant women are exposed to a range of phthalates in personal and home care products. Available data on the levels of phthalates in urine provide physicians with a reference range so that they can determine whether patients have been exposed to higher levels of phthalates.[11,12]

Another class of environmental chemicals being passed from mothers to infants is polybrominated diphenyl ethers (PBDEs). These suspected neurotoxicants came into use over the last two decades as flame retardants. They are used in many household products, including carpets, furniture cushions and construction materials. It is unclear how widespread exposure to PBDEs is in the United States, but there is evidence that U.S. exposure is among the highest in the world.[13-15]

Experimental studies show that PBDEs disturb the balance of thyroid hormones, upon which brain development depends. Changes in thyroid hormone levels adversely affect postnatal development in humans, including growth, hearing and mental acuity. In this regard, it should be noted that some 116 environmental chemicals have been reported to affect production, transport or metabolism of thyroid hormones. For instance, perchlorate, used as an oxygen source in missile and rocket fuel, is common in drinking water in the southwestern United States. It inhibits iodine uptake by the thyroid. Other environmental agents and foods are thyroid-disrupting. Some of these toxicants adversely affect thyroid function by more than one mechanism. Moreover, a critical question is whether the combinations of toxicants have synergistic effects or sometimes cancel each other out. Further, screening for thyroid disruption does not occur primarily because there is no definitive, easily measurable biological endpoint apart from triiodothyronine (T3), tetraiodothyronine (T4) and thyroid-stimulating hormones (TSH) serum concentration.

It is clear that the thyroid system is so complex that understanding its normal function is difficult. Even more difficult is sorting out environmentally induced disruptions.

One of the more challenging aspects of fetal exposure is the effects of a number of environmental stressors on gestational molding that might lay dormant for decades. In this regard, many diseases are thought to arise through a series of changes within cells that require a number of years to evolve from initiation to actual manifestation of illness. Several epidemiological studies now point to this conclusion.[16-18] These studies have fueled efforts to uncover the molecular actions that can go awry early on in the fetal environment and prompt dysfunctions—cardiovascular disease, type-2 diabetes, hypertension—decades later. Investigations are focusing on a number of environmental factors: maternal stress and level of protein in maternal diet, among other factors.

The interest in parental stress factors is intense. Cory-Slechta's group[19] has observed in experimental work interactions of lead and stress, confirming the hypothesis that lead and stress interact. Among the significant findings was that developmental lead exposure per se increased the level of corticosterone, the main glucocorticoid of the experimental animal. This finding concurs with other studies that demonstrated permanent changes in offspring corticosterone concentrations resulting from prenatal stress. The interactions of lead and stress are not easily predictable and have significant implications for human health risk assessment. It should also be noted that stress hormones, such as cortisol, are known as powerful regulators of gene expression. These hormones might well turn on and off genes critical to fetal development of organs, such as the kidney, further contributing to later disease. For example, a poorly formed kidney might falter in regulating blood pressure.

However, bewildering to researchers is that many healthy (stress-free) women give birth to infants whose growth is somehow retarded in the womb, indicating that it is not only the mother's condition that matters but what (such as environmental agents) reaches her fetus through the placenta.[20] Little is known about placental development and defects, attributable to environmental influences. Anatomically, the placenta consists of a number of cell layers interposed between the fetal and maternal circulation. As pregnancy progresses, there is contact between fetal blood and the syncytiotrophoblast—the placental cell layer most important to placental function and maternal-fetal exchange. This leads to a greater exchange of environmental chemicals across the placenta, as gestation proceeds. Influencing placental transfer of environmental toxicants are uterine/placental blood flow, placental permeability and placental metabolism.[21,22] The exact relationship of the number of cellular layers of the placenta to its permeability has not been thoroughly investigated. Currently, it is not considered to be of primary importance in determining the distribution of environmental toxicants in the fetal system.

Another concern is the susceptibility of developing fetus and neonate to chemical carcinogens, because the reported incidence of childhood cancer has increased in the past two decades. From 1973 to 1944, the incidence of brain cancer increased by 39.6%, with nearly equal increases in boys and girls.[23]

Cancers that arise in the pediatric age group differ from those that occur among adults. This difference is

in the distributions of anatomic sites of involvement, as well as predominant histological patterns. For example, malignancies of epithelia tissues are common among adults but occur rarely among children. Conversely, tumors in young children often are composed of embryonal cell types, which are uncommon among malignancies of adults.

When compared to adults, children younger than 2 face a 10-fold risk of developing cancer if they are exposed to some environmental agents. Experimental and human evidence indicates that the developing fetus has heightened susceptibility to certain environmental carcinogens compared with adults. Positive association has been observed between pesticide use in the home or garden, and childhood leukemia and brain cancer.[24] Studies have consistently implicated pesticides exposure in the development of leukemia, central nervous system tumors and neuroblastoma.[25] Parental occupational exposure to pesticides has also been linked to childhood cancer. In addition to pesticide risks, father's preconception occupational exposure to radiation has been associated with increased incidence of leukemia.[26] An increased risk of leukemia in children who were exposed to diagnostic irradiation in utero was first reported in 1956.[27] Other parental occupations implicated in the occurrence of childhood cancers include medical and dental professions, as well as parental employment in the aircraft industry.[28,29]

In North Carolina, increased childhood cancer mortality for leukemia was found in neighborhoods with high average groundwater radon concentrations.[30]

Internationally, mean indoor radon concentrations also have been correlated with childhood cancer incidence.

A number of factors may enhance fetal susceptibility to environmental carcinogens. These factors include higher rates of cell proliferation, the greater number of target cell at risk, lower immunologic competence, and decreased capacity to activate and detoxify carcinogens as well as to repair DNA.

Recently, molecular epidemiologic studies demonstrated that exposure to common environmental pollutants in urban communities can act in combination to adversely affect fetal development. For instance, a study found an association between environmental tobacco smoke (ETS), benzo[a]pyrene (BaP), other polycyclic aromatic hydrocarbons (PAH) and two birth outcomes: decreased birthweight and smaller head circumference.[31] Both have been correlated with lower IQ and poorer cognitive function and school performance. ETS, a complex mixture of >4,000 chemicals, can adversely affect fetal growth as well as child growth and development. Indeed, the adverse effects of nicotine on fetal growth are well-documented. The posited mechanisms underlying these effects include estrogenic effects, induction of P450 enzymes and DNA damage resulting in activation of apoptotic pathways. For clinicians attempting to establish a causal relationship, it is important to know that neither nicotine nor cotinine is usually present in body fluids in the absence of exposure to tobacco smoke, although unusually large intakes of some foods could produce measurable levels of nicotine and cotinine. Urinary cotinine levels in infants increase with the number of cigarettes smoked by the mother. Significantly, there is evidence that the clearance of nicotine and cotinine is reduced during fetal development, thus, prolonging the duration of exposure. In addition to transfer from the maternal circulation, the fetus is exposed from gastrointestinal reabsorption of environmental toxicants in swallowed amniotic fluids.

A new addition to the ETS health effects database is a study of ETS exposure on sickle cell disease.[32] Children with the disease who are exposed to ETS tend to have more than twice as many "crises"—including vaso-occlusive pain and acute chest syndrome—as patients not exposed. Environmental tobacco smoke increases the risk of crises by 90% among children with sickle cell disease.

Polycyclic aromatic hydrocarbons, such as BaP, which arises from incomplete combustion of plant and animal material, are endocrine disruptors. In addition to being genotoxic and carcinogenic, endocrine disruptors are environmental chemicals that have the capacity to block or modulate the synthesis, release, transport, metabolism, binding or elimination of natural hormones. The results of endocrine disruption may not be easily detected. The effects may be subtle and delayed in onset and may not necessarily be clinically evident in the exposed individual but rather in offspring. Considerable attention has been allotted to endocrine disruption problems. The focus is on estrogenic, antiestrogenic or antiandrogenic actions of various environmental pollutants. One piece of data from recent experimental evidence suggests that abnormal bone composition may be an outcome of human exposure to mixtures of endocrine disruptors. A possible mechanism is inhibition of osteoclastic activity (bone resorption is accomplished by osteoclasts, one of the main types of bone cells).[33]

Breast Milk Exposure

At another level of maternal and child interaction, infants may be exposed to environmental chemicals through breast milk. Breast milk is not contaminant-free, and contamination of this source of nutrition for infants is widespread, the consequence of decades of inadequately controlled pollution, including environmental toxicants. Although most breastfeeding mothers have detectable levels of several environmental agents

in their milk, there are no established normal or abnormal values for clinical interpretations. There is limited data on organic environmental chemicals in breast milk in the United States. In Canada, surveys reveal in breast milk levels of flame retardant, polybrominated biphenyl ethers, three times higher than in the United Kingdom and Germany. Canadian levels are still lower than those in the United States, where PBDE contamination levels now double every five years. PBDEs bioaccumulation and they are known developmental toxicant in animals. A challenging unknown is the precise health outcome in infants exposed to environmental toxicants via breast milk. Thus,far, effects on the nursing child have been seen primarily in high-dose poisoning in which the mother was clinically ill. Still further, it is clear that heavy metals, including lead, cadmium and mercury, appear in milk in smaller concentration than lipid-soluble environmental chemicals. This is attributed to metals' low level of lipid solubility and high binding to erythrocytes. Thus, the amount of heavy metal exposure to the infant appears to be low in comparison to other sources. There are other factors that influence the transfer of chemicals through breast milk: maternal physiology, such as adipose tissue levels; age; parity; milk composition and volume; and breastfeeding patterns. Today, in preventive medicine, there is general agreement that breastfeeding can be beneficial to infants, but a better understanding of an infant's level of exposure to environmental toxicants by the breast milk route is essential.

Physical Locations

Pediatricians will want to be equipped to advise parents of potential environmental risks in a range of physical settings. In this direction, exposure studies are increasingly drawing attention to the health hazards in physical locations of children: homes, daycare centers, schools, and undesirable neighborhood facilities and vacant lands. Exposure to these environments changes with stages of development, which may cause variations in the environmental risk scenarios. Schools may be a major source of exposure to cat and dog allergens for children who do not have these pets at home. Surveys have found poor air quality in schools attributable to inadequate ventilation systems.

Newborns frequently spend more time in a single environment for prolonged periods rather than several different environments. Infants and toddlers are frequently on the floor or carpet or grass. Here, they have more potential exposure to contaminants associated with such surfaces. Surfaces, such as soft plush toys and polyurethane foam furniture, can also serve as reservoirs for applied pesticides. Wall-to-wall carpeting can also serve as a reservoir for pollutants. Such contaminants include dust mites, bacteria and asthma-inducing allergens, as well as pesticide residues, a source of which is "take-home" exposure among workers. The hypothesis has been consistently supported that the take-home exposure pathway contributes to residential pesticide contamination, where young children are present. An equally significant risk factor is home dampness, which has been consistently shown to be associated with respiratory symptoms and asthma. Recent studies point to mold exposure as a factor in asthma development. In these studies, mold effects were the most pronounced among infants whose mothers had asthma.[34]

Not to be overlooked is the prevalence of lead-based paint in U.S. housing, which continues to increase the risk of childhood lead poisoning. Despite a large decline in the number of such housing, there are still millions of housing with lead hazards. Within the past decade, concerns about lead dust on interior surfaces have intensified by the massive demolition of older structures in urban neighborhoods.

Of particular relevance to pediatric care in today's urban neighborhoods is a study of demolition and debris removal in Baltimore, MD.[35] That study found that urban renewal activities were associated with increases in lead dust fall. Other cities (Washington, DC; Atlanta; and Chicago) are in the midst of demolition and redevelopment programs. From these activities, lead-contaminated dust can be tracked into houses on shoes and or blown into houses. Under these circumstances, the likelihood and frequency of a child's exposure to lead in dust is greater for interior (in-home) surfaces than exterior surfaces. Most demolition of aging and derelict housing is in neighborhoods where children are already at high risk of lead poisoning. Interestingly, just when textbooks were reporting most municipal water supplies measured at tap contain less than 0.05 microgram per milliliter; the District of Columbia water authorities were recording (2003–2004) measurements thousands of times higher at the taps in home in the nation's capital. Robust databases continue to make clear that there is no threshold for lead effects on the brain, and small amounts seem to have relatively large effects.

Also in the home, the pediatric population is potentially exposed to a number of combustion gases—respiratory irritants. Oil- and gas-fired furnaces, water heaters, ovens, charcoal grills and fireplaces all produce combustion gases. These gases may include carbon monoxide (CO), carbon dioxide, sulfur dioxide, water vapor, hydrogen cyanide, formaldehyde and various hydrocarbons. Often overlooked in clinical settings are symptoms of chronic exposure to low levels of CO, including poor vision, retinal hemorrhaging and behavioral impairment. Dozens of different volatile organic compounds (VOCs) have been measured in indoor air. They are from a variety of

sources, including cleaning agents, paints, fragrances, fingernail polish and hardener. Many of these products emit formaldehyde, an irritant to the conjunctiva, and the upper and lower respiratory system.

Resources

In addition to the usual methods of clinical diagnosis, a number of tools can assist the clinician in an assessment and in the management of environmentally related disorders in children. For instance, the interpretation of information from basic evaluations (e.g., physical examination, laboratory evaluations) can be enhanced by existing and emerging databases. Within the past two years, the Centers for Disease Control and Prevention (CDC) have provided a vital tool for clinicians and researchers on children's environmental health risks. The CDC National Report on Human Exposure to Environmental Chemicals is the broadest study yet of chemicals that Americans absorb in their bodies.[36] Among the findings, the new study disclosed that children had higher levels of residues from secondhand smoke and plastics than adults. Historically, estimates of human exposure to toxic chemicals have been based on concentration of these chemicals in environmental media, such as air, water, food, along with assumption about how children are exposed. The CDC database, available on the Internet (www.atsdr.gov/toxfaq.html) is useful to pediatricians in determining whether a child has an unusually high exposure level. In other words, it is important to mesh a child's health appraisal with environmental data.

The CDC report on human exposure reflects advances in laboratory technology and molecular biology. These developments have provided new tools for measuring a broad range of chemicals in human tissues—tools that can help pediatricians assess how much of an environmental agent has been absorbed in the patient's body. Encouragingly, methods have been developed to measure smaller levels of environmental toxicants in tissues, as well as the ability to do so with smaller samples.

Moreover, the identification of genes responsible for human Mendelian diseases, once a substantial task, can now be routinely accomplished in a shorter period. One result has been an expansion of the list of diseases that can be detected by gene analysis. It is possible to perform DNA tests for more than 30 diseases within a few days of birth, opening the way for early intervention, such as the avoidance of environmental triggers.

Further, with the expansion of new technologies in the last two decades, the field of biomarker development and application has assumed greater significance than in the past. Because individuals process environmental exposures differently, the use of such markers may provide a more accurate measurement of relevant exposure to an environmental agent. An example of this type of marker is the use of protein and/or DNA adducts, usually measured in blood, serum, urine or exfoliated cells. Another example is cotinine, a metabolic product of nicotine. Cotinine, which is toxic to children and can lead to serious medical complications, can be found in the urine of children who have been exposed to environmental tobacco smoke. With biomarkers, it is possible to intervene early and prevent progression of the disease to an irreversible level. Biomarkers can be added to the hierarchy of prevention and can be thought of as supplementary to the traditional pediatric practice, not as a replacement.

Another valuable resource for dealing with pediatric environmental health problems is the national network of pediatric environmental health specialty units. These services are located throughout the United States as well as Canada and Mexico. Established in response to growing concerns about pediatric environmental health, these government-funded units are staffed by professionals in pediatrics, toxicology, epidemiology and occupational/environmental medicine. They provide telephone consultations, receive clinical referrals and conduct training in the diagnosis and treatment of illnesses that are or may be associated with exposure to environmental agents. Some 11 pediatric environmental health units were in operation in the United States in 2004.[37]

Still, another resource is the Centers for Children's Environmental Health and Disease Prevention Research. These centers promote the translation of basic research finding into applied intervention and prevention methods. The centers, supported by federal health agencies, maintain close ties with community organizations that assist in the dissemination of children's health research findings to the community.

Comment

The sum vector of the topics discussed in the preceding paragraphs is a clear indication that pediatric environmental health is taking on immensely increased importance. Why? It is abundantly clear that the major problem of children (nationally and globally) is, to one degree or another, caused, mediated or aggravated by environmental factors. It is equally clear that physicians, truly wanting to meet the healthcare needs of children, must be aware of the patient's environmental contexts.

Biomedical advances thus far indicate the logic of anticipating that our understanding of how children's health may be influenced by environmental factors will continue to improve as more research evolves. This understanding will also be advanced by better information on disease mechanisms and pathways at the molecular level. Without question,

complex diseases, with multiple susceptibility determinants (both environmental and genetic), will take time to dissect. But the process will be aided by effective technology transfer and feedback to ensure wider application of advances in pediatric environmental health. A good start has been made, as the American Academy of Pediatrics and other organizations and agencies that provide guidance on pediatric health issues have put environmental health high on their agenda. These groups strongly suggest that no physician's education would be complete without an understanding of the role played by environmental factors in human health and diseases and knowledge of ways in which these factors can be modified to the benefit of children.

ACKNOWLEDGEMENTS

This paper was presented at Howard University Hospital's Pediatrics Grand Rounds, January 30, 2004, under the direction of the Department of Pediatrics, Renee Jenkins, MD, professor and chair.

REFERENCES

1. Lubin B, Lewis R. Biomarkers and pediatric environmental health. *Environ Health Perspect.* 1995;103(suppl 6)99-104.

2. Amler RW, Gitterman BA. Pediatricians can turn to specialty units for advice on environmental health. *APP News.* January 2004.

3. Childs B. Genetic Medicine, a Logic of Disease. Baltimore Johns Hopkins University Press, 1999.

4. Robert R, Rodriquez W, Murphy D, et al. Pediatric labeling. *JAMA.* 2003;290: 905-911.

5. Rogan WJ. Environmental poisoning of children—lesson from the past. *Environ Health Perspect.* 1995;103(suppl 619-23.

6. Funatsu I, Yamashita F, Ito Y. Polychlorobiphenyls (PCB)-induced fetopathy Clinical observation. *Kurume Med J.* 1972;19:43-51.

7. Whyatt RM, Camann DE, Kinney PL, et al. Residential pesticide use during pregnancy among a cohort of urban minority women. *Environ Health Perspect.* 2002;110:507-514.

8. Aldridge JE, Seidler FJ, Slokin TA. Developmental exposure to chloropyrifos elicits sexual-selective alterations of serotonergic synaptic function in adulthood: critical periods and regional selectivity for effects of the serotonin transporter, receptor sutypes and cell signaling. *Environ Health Perspect.* 2004;112:149-155.

9. Faustman EM. Mechanisms underlying children's susceptibility to environmental toxicants. *Environ Health Perspect.* 2000;108(suppl 1)13:-21.

10. Institute of Medicine of Medicine. Neurological, Psychiatric and Developmental Disorder. Washington, DC. National Academy Press, 2002.

11. Centers for Disease Control and Prevention. Second National Report on Human Exposure to Environmental Chemicals, Atlanta. National Center for Environmental Health 2003.

12. Blount BC, Silva MJ, Caudill SP, et al. Levels of seven urinary phthalate metabolites in a human reference population. *Environ Health Perspect.* 2000;108:979-982.

13. Betts KS. Rapidly rising PBDE levels. Farfel MR, Orlova AO, Lees PSJ, Rhode C, Ashley PH, Chisolm JJ. A study of urban housing demolition as sources of lead in ambient dust: demolition practices and exterior dust. *Environ Health Perspect.* 2003;111:1128-1134. North America. *Environ Sci Technol.* 2002;36: 50A-52A.

14. deWit CA, An overview of brominated flame retardants in the environment. *Chemosphere.* 2002;46:583-624.

15. Rahman F, Langford KH, Scrimshaw MD, et al. Polybrominated diphenyl ether (PBDE) flame retardants. *Sci Tech Environ.* 2001 257:1-17.

16. Barker, DJ. Fetal origins of cardiovascular disease. *Ann Med.* 199 31:3-6.

17. Ekbom A, Hsieh CC, Lipworth L, et al. Trichopoulos D, Intrauterine environment and breast cancer risk in women: a population–based study. *J Natl Cancer Society.* 89:71-76.

18. Cory-Schlecter, DA, Virgolini. MB, Thiruchelevan M, et al. Maternal stress modulates the effects of developmental lead exposure *Environ Health Perspect.* 2004112:717-729.

19. Couzin J, Quirks of the fetal environment felt decades later. *Science.* 2002;296:2167-2169.

20. Schecther CB. Re brain and other central nervous system cancers: recent trends in incidence and mortality. *J Natl Cancer Inst.* 1999;91:2050-2051.

21. Ginsberg G, Slikker W, Bruckner J, et al. Incorporating children's toxicokinetics into a risk framework. *Environ Health Perspect.* 2004;112:272-283.

22. Adinolfi M, The development of the human blood-CSF- brain barrier. *Dev Med Child Neurol.* 1985;27:532-537.

23. Reis L, Eisner M, Kosary C, et al. Seer Cancer Statistics Review, 1975–2000. Bethesda, MD National Cancer Institute.

24. Pogoda JM, Preston-Martin S. Household pesticides and risk of pediatric brain tumors. *Environ Health Perspect.* 1997;105:1214-1220.

25. Zahm SH, Ward MH, Pesticides and childhood cancer. *Environ Health Perspect.* 1998;106(suppl 3)893-908.

26. Savitz DA, Chen J. Parental Occupation and Childhood Cancer: review of epidemiologic studies. *Environ Health Perspec.* 1990;88:325-337.

27. Stewart A, Webb J, Giles D. Malignant disease in childhood and diagnostic irradiation in utero. *Lancet.* 1956;2:447.

28. Adundal SE, Kinner-Wilson LM. Parental occupations and cancers: a review of the literature. *J Epidemiol Community Health.* 1986;40:30-36.

29. Kuijten RR, Bunin GR, Nass CC. Parental occupation and childhood astrocytoma: results of a case–control study. *Cancer Res.* 1992;52:1887-1893.

30. Collman GW, Looms DP, Sandler DP. Childhood cancer mortality and radon concentration in drinking water in North Carolina. *Br J Cancer.* 1991; 63;626-629.

31. Berkowitz GS, Wetmur JG, Burman-Deych E, et al. In utero pesticide exposure, maternal paraoxnase activity and head circumference. *Environ Health Perspect.* 2004;112: 388-391.

32. West DC, Pattrick R, Rahman A, et al. Impact of environmental tobacco smoke on children with sickle cell disease. *Arch Pediatr Adoles Med.* 2003;157:1107-1201.

33. Lacey DL, Tan HL, Lu J. Osteoprotegerin ligarad modulates murine osteoclast survival ion vitro and in vivo. *Am J Pathol.* 2000;157:435-440.

34. Gent JF, Rent P, Belanger K, et al. Level of household mold associated with respiratory symptoms in the first year of life in a cohort risk of asthma. *Environ Health Perspect.* 2002;110:A781-A785.

35. Farfel MR, Orlova AO, Lees PSJ, et al. A study of urban housing demolition as sources of lead in ambient dust: demolition practices and exterior dust. *Environ Health Perspect.* 2003;111:1128-1134.

36. Centers for Disease Control and Prevention Second National Report on Human Exposure to Environmental Chemicals. Atlanta, GA National Center for Environmental Health 2003.

37. Amler RW, Gitterman BA. Pediatrician can turn to specially units for advice on environmental health. *APP News.* January 2004. ■